This will relate to frequency of administration of this drug to cancer patients. SEQ ID NO: 27 (5'-TsCsCs GsTsCs AsTsCs GsCsTs CsCsTs CsAsGs GsG-3') is currently under evaluation in *ras* dependent tumor models (Cowsert, L.M. *Anti-cancer drug design*, **1997**, *12*, 359-371). The parent compound, SEQ ID NO: 27, is in Phase I clinical trials against solid tumors by systemic infusion.

[0285] Antisense oligonucleotides having the 2'-Me modification are prepared and tested in the aforementioned assays in the manner described to determine activity.

[0286] Ha-ras Antisense Oligonucleotides with chimeric C3'-endo and C2'-endo modifications and Their Controls.

Table XVI
***Ha-ras* Antisense Oligonucleotides With chimeric C3'-endo and C2'-endo modifications and Their Controls.**

SEQ ID NO:	Sequence	Backbone	2'-Modif.	Comments
27	5'-TsCsCs GsTsCs AsTsCs GsCsTs CsCsTs CsAsGs GsG-3'	P=S	2'-H	parent
28	5'-TsCsAs GsTsAs AsTsAs GsGsCs CsCsAs CsAsTs GsG-3'	P=S	2'-H	mismatch control
29	5'-ToToCo GsTsCs AsTsCs GsCsTs CoCoTo CoAoGo GoG-3'	P=O/P=S/ P=O	2'-O-Moe in wings (Mixed Backbone)	Parent Gapmer
27	5'-TsCsCs GsTsCs AsTsCs GsCsTs CsCsTs CsAsGs GsG-3'	P=S	2'-O-MOE in wings uniform	Parent Gapmer as thioate

29	5'-ToCoAo GsTsAs AsTsAs GsCsCs GsCsCs GsCoCo CoCoAo CoAoTo GoG-3'	P=O/P=S/ P=O	2'-O-MOE in wings	Parent Gapmer (mixed Backbone)
28	5'-TsCsAs GsTsAs AsTs As GsCsCs GsCsCs CsCsAs CsAsTs GsC-3'	P=S	2'-O-MOE in wings	Control Gapmer as uniform Thioate
27	5'-TsCsCs GsTsCs AsTsCs GsCsTs CsCsTs CsAsGs GsG-3'	P=S	2'-O-MOE in wings	Control Gapmer with MOE control
28	5'-TsCsAs GsTsAs AsTsAs GsCsCs GsCsCs CsCsAs CsAsTs GsC-3'	P=S	2'-O-MOE in wings	Control Gapmer with MOE Control

All underlined portions of sequences are 2'-Me.

PROCEDURE 7

***In vivo* nuclease resistance**

[0287] The *in vivo* Nuclease Resistance of chimeric C3'-endo and C2'-endo modified oligonucleotides is studied in mouse plasma and tissues (kidney and liver). For this purpose, the C-raf oligonucleotide series SEQ ID NO: 30 are used and the following five oligonucleotides listed in the Table below will be evaluated for their relative nuclease resistance.

Table XVII
Study of *in vivo* Nuclease Resistance of chimeric C3'-endo (2'-O-MOE) and C2'-endo (2'-S-Me) modified oligonucleotides with and without nuclease resistant caps (2'-5'-phosphate or phosphorothioate linkage with 3'-O-MOE in cap ends).

SEQ ID NO:	Sequence	Backbone	Description
30	5'-ATG CAT TCT GCC CCA AGGA-3'	P=S, 2'-H	(control) rodent C-raf antisense oligo
31	AoToGo CoAsTs TsCsTs GsCsCs CsCsAo AoGoGo A	P=O/P=S/P=O	2'-MOE/2'-S-Me/ 2'-MOE
32	AsTsGs CsAsTs TsCsTs GsCsCs CsCsAs AsGsGs A	P=S	2'-MOE/2'-S-Me/ 2'-MOE
33	Ao*ToGo CoAsTs TsCsTs GsCsCs CsCsAo AoGoGo *A	P=O/P=S/P=O	In asterisk, 2'-5' linkage with 3'-O-MOE;2'-O-MOE/2'-S-Me/2'-O-MOE/2'-5' linkage with 3'-O-MOE in asterisk;
34	As*TsGs CsAsTs TsCsTs GsCsCs CsCsAs AsGsGs *A	P=S	In asterisk, 2'-5' linkage with 3'-O-MOE;2'-O-MOE/ 2'-S-Me/2'-O-MOE/2'-5' linkage with 3'-O-MOE in asterisk.